

Amendments to the Claims:

1. - 26. (Canceled).
27. (Original) A method of treating or preventing a pathology associated with a GPCR, said method comprising administering a chimeric polypeptide to a subject in which such treatment or prevention is desired in an amount sufficient to treat or prevent said pathology in said subject, wherein the chimeric polypeptide comprises a first domain consisting essentially of a third intracellular loop (i3 loop) or a fragment thereof of a G protein coupled receptor (GPCR), and a second domain, attached to the first domain, wherein the second domain is a naturally or non-naturally occurring cell-penetrating, membrane-tethering hydrophobic moiety, wherein the first domain does not comprise a native extracellular ligand of the GPCR and wherein the chimeric polypeptide binds to its cognate GPCR.
28. (Original) The method of claim 27, wherein said subject is a human.
29. (Canceled).
30. (Canceled).
31. (Canceled)
32. (Withdrawn) The use of a therapeutic in the manufacture of a medicament for treating a syndrome associated with a human disease, the disease selected from a pathology associated with a chimeric polypeptide, wherein the therapeutic is the chimeric polypeptide, which comprises a first domain consisting essentially of a third intracellular loop (i3 loop) or a fragment thereof of a G protein coupled receptor (GPCR), and a second domain, attached to the first domain, wherein the second domain is a naturally or non-naturally occurring cell-penetrating, membrane-tethering hydrophobic moiety, wherein the first domain does not comprise a native extracellular ligand of the GPCR and wherein the chimeric polypeptide binds to its cognate GPCR.

33. (Canceled).
34. (Original) A method of treating a pathological state in a mammal, the method comprising administering to the mammal a chimeric polypeptide comprising a first domain consisting essentially of a third intracellular loop (i3 loop) or a fragment thereof of a G protein coupled receptor (GPCR), and a second domain, attached to the first domain, wherein the second domain is a naturally or non-naturally occurring cell-penetrating, membrane-tethering hydrophobic moiety, wherein the first domain does not comprise a native extracellular ligand of the GPCR and wherein the chimeric polypeptide binds to its cognate GPCR.
35. (Original) The method of claim 27, wherein said hydrophobic moiety is attached at the N-terminal end, the C-terminal end, or both the N-terminal and C-terminal ends of said first domain.
36. (Original) The method of claim 27, wherein said hydrophobic moiety is a lipid.
37. (Original) The method of claim 36, wherein said hydrophobic moiety is selected from the group consisting of: capryloyl (C₈); nonanoyl (C₉); capryl (C₁₀); undecanoyl (C₁₁); lauroyl (C₁₂); tridecanoyl (C₁₃); myristoyl (C₁₄); pentadecanoyl (C₁₅); palmitoyl (C₁₆); phtanoyl ((CH₃)₄); heptadecanoyl (C₁₇); and stearyl (C₁₈), wherein said hydrophobic moiety is attached to said chimeric polypeptide with amide bonds, sulfhydryls, amines, alcohols, phenolic groups, or carbon-carbon bonds.
38. (Original) The method of claim 27, where said i3 loop or fragment thereof comprises at least 3 contiguous amino acid residues of the third intracellular loop.
39. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises at least 5 contiguous amino acid residues of the third intracellular loop.
40. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises at least 7 contiguous amino acid residues of the third intracellular loop.

41. (Original) The method of claim 27, wherein said first domain comprises a protease-activated receptor (PAR) and said second domain comprises a lipid moiety.
42. (Original) The method of claim 27, wherein the G-protein coupled receptor or fragment thereof, is selected from the group consisting of a luteinizing hormone receptor, a follicle stimulating hormone receptor, a thyroid stimulating hormone receptor, a calcitonin receptor, a glucagon receptor, a glucagon-like peptide 1 receptor (GLP-1), a metabotropic glutamate receptor, a parathyroid hormone receptor, a vasoactive intestinal peptide receptor, a secretin receptor, a growth hormone releasing factor (GRF) receptor, protease-activated receptors (PARs), cholecystikinin receptors, somatostatin receptors, melanocortin receptors, ADP receptors, adenosine receptors, thromboxane receptors, platelet activating factor receptor, adrenergic receptors, 5-HT receptors, CXCR4, CCR5, chemokine receptors, neuropeptide receptors, opioid receptors, parathyroid hormone (PTH) receptor, and vasoactive intestinal peptide (VIP) receptor.
43. (Original) The method of claim 27, wherein said G-protein coupled receptor is a mammalian G-protein coupled receptor.
44. (Original) The method of claim 37, wherein said hydrophobic moiety is palmitoyl.
45. (Original) The method of claim 27, wherein said G-protein coupled receptor is a protease-activated receptor (PAR).
46. (Original) The method of claim 45, wherein the protease-activated receptor is selected from the group consisting of PAR1, PAR2, and PAR4.
47. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises a sequence selected from the group consisting of SEQ ID NO: 1-16, 19-23, and 29.

48. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises a sequence selected from the group consisting of SEQ ID NO: 1-10, and 23.
49. (Original) The method of claim 27, wherein the said G-protein coupled receptor is selected from the group consisting of CCKA, CCKB, SSTR2, and SubP receptors.
50. (Original) The method of claim 36, wherein said hydrophobic moiety is a steroid.
51. (Original) The method of claim 27, wherein said hydrophobic moiety is selected from the group consisting of a phospholipid, a steroid, a sphingosine, a ceramide, an octyl-glycine, a 2-cyclohexylalanine, and a benzoylphenylalanine.
52. (Original) The method of claim 27, further comprising a third domain, said third domain being a cell-penetrating, membrane tethering hydrophobic moiety attached to said first domain.
53. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:1.
54. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:2.
55. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:3.
56. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:4.
57. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:5.
58. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:6.

- 59. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:7.
- 60. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:8.
- 61. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:9.
- 62. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:10.
- 63. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:11.
- 64. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:12.
- 65. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:13.
- 66. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:14.
- 67. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:15.
- 68. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:16.
- 69. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:19.
- 70. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:20.

71. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:21.
72. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:22.
73. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:23.
74. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:28.
75. (Original) The method of claim 27, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:29.
76. (Original) The method of claim 27, wherein the hydrophobic moiety is a steroid.